



Clinicopathological features and survival outcomes of pediatric mediastinal tumors: A 10-year retrospective study

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Abstract

Background: Primary mediastinal masses account for 3% of all chest tumors. Owing to their heterogeneous clinical presentations and the need for precise diagnosis, this study evaluated the clinicopathological features and survival outcomes of children with primary mediastinal masses admitted to Shahid Sadoughi Hospital, Yazd, Iran, between 2011 and 2021.

Methods: In this descriptive cross-sectional study, 17 children under 18 years of age with primary mediastinal masses were evaluated using census sampling. Data were collected with a checklist that included age, sex, tumor location, presenting symptoms, tumor type, treatment received, and malignancy status. Prognosis and survival were subsequently assessed. Statistical analysis was performed using SPSS 22, with Kaplan-Meier and Log-rank tests applied for survival assessment.

Results: Among the 17 patients, 12 (70.6%) were girls and 5 (29.4%) were boys. Five patients (29.4%) died during follow-up. Nine tumors (53%) were benign and eight (47%) were malignant. Ganglioneuroma was the most frequent tumor type (29.4%). Survival analysis showed no statistically significant association between survival and surgery ($P=0.222$), malignancy status ($P=0.158$), neural origin ($P=0.666$), chemotherapy ($P=0.057$), radiotherapy ($P=0.752$), tumor location ($P=0.661$), sex ($P=0.670$), or age ($P=0.877$).

Conclusion: The findings suggest that the distribution of histological types of primary mediastinal masses in children is influenced by anatomical location. However, age, sex, treatment type, and tumor location were not significantly associated with survival outcomes in this cohort.

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Introduction

The mediastinum is the central thoracic cavity located between the pleural cavities. It is bounded inferiorly by the diaphragm, superiorly by the thoracic outlet, anteriorly by the sternum, and posteriorly by the vertebral bodies and paravertebral regions (1). Anatomically, it is divided into four compartments: superior, anterior, middle, and posterior, each containing distinct structures. Therefore, masses arising from these structures may differ in origin and tend to involve specific compartments (2). Primary mediastinal masses account for 3% of all chest tumors, with an average annual incidence of 8 cases per 1 million people. These masses may be benign or malignant and, depending on their primary or secondary origin, may arise from thymic, hematopoietic, lymphatic, germinal, neurogenic, or mesenchymal tissues (3). Mediastinal lesions encompass a broad histopathological and radiological spectrum, including benign, malignant, infectious, and reactive masses that may occur at any age (4). Fibromas, lipomas, and malignant tumor types may be observed in all three compartments (1,5).

Age-related differences exist in tumor biology, host characteristics, and treatment protocols for mediastinal lesions. Thymoma, neurogenic tumors, and benign cysts are among the most common mediastinal lesions, accounting for 60% of cases (4). In the study by Davis (1987), which included 400 cases of mediastinal masses, the most common primary tumor was thymic neoplasm (17%), followed closely by lymphoma (16%), nerve tumor (14%), and germ cell tumor (11%) (6). Whooley et al. (1999) reported that 63.8% of tumors were located in the anterior mediastinum, 22.9% in the posterior mediastinum, and 13.3% in the middle mediastinum. In that study, lymphoma was the most common primary mediastinal tumor, with a frequency of 21.9%, followed by thymoma at 18.1% (7).

Patients may be asymptomatic, and mediastinal masses may be detected incidentally on routine chest radiography performed for other reasons (3). In a United States study of 73 patients, 46.6% were symptomatic. The most common symptoms included chest pain, myasthenia gravis, superior vena cava obstruction, hoarseness, upper-limb pain, dysphagia, and shortness of breath (8). Some masses may also cause endocrine syndromes, including hypertension, hypercalcemia, thyrotoxicosis, and gynecomastia (5). Given the variability of symptoms across different types of mediastinal masses and the importance of accurate diagnosis, this study examined the clinicopathological characteristics and survival outcomes of primary mediastinal masses in children referred to Shahid Sadoughi Hospital in Yazd from 2011 to 2021.

Methods

This was a descriptive, cross-sectional, retrospective study. Sampling was performed by census and included all patients under 18 years of age who were diagnosed with primary mediastinal tumors, underwent biopsy, and had samples submitted to the pathology department of Shahid Sadoughi Hospital in Yazd between January 1, 2011, and December 31, 2021. The sample size consisted of 17 patients. Individuals with insufficient clinical, demographic, or pathological information, as well as those diagnosed with other types of cancer, were excluded from the study. The research was initiated after approval was obtained from the Ethics Committee of the School of Medicine at Shahid Sadoughi University of Medical Sciences, under ethical code IR.SSU.MEDICINE.REC.1399.273. Patient files were reviewed, and data on age, gender, pathology reports, initial clinical symptoms, anatomical tumor location, type of treatment received, and contact

numbers were extracted. Additional clinical information, including treatment type, survival status, and, in the event of death, the cause of death - specifically whether death was attributable to the primary mediastinal tumor with the indicated histological type - was obtained from patient records and telephone follow-up. All patients were followed until death or the 20th of March 2021.

Cancer-specific survival was estimated from the time of diagnosis until death due to the primary mediastinal tumor with the indicated histological type or until the last follow-up (March 2021). Overall survival (OS) was calculated from the time of diagnosis of the primary mediastinal tumor with the indicated histological type until death from any cause or the last follow-up (March 2021). After data collection and validation, the information was entered into SPSS software version 22. Percentages, means, and standard deviations were used for descriptive analysis. Frequency distributions were compared using the Chi-square test, and mean values were compared using the T-test. Patient survival was evaluated using Kaplan-Meier curves, and survival comparisons between groups were analyzed using the Log-rank test. In all analyses, a p-value of <0.05 was considered statistically significant.

Results

This study was conducted to investigate the clinicopathological characteristics and survival outcomes of primary mediastinal masses in children referred to Shahid Sadoughi Hospital, Yazd, and included 17 patients with primary mediastinal tumors (PMT) from 2011 to 2021. The patients' ages ranged from 1 month to 16 years. Among the 17 children

studied, 12 (70.6%) were girls and 5 (29.4%) were boys. Chi-square analysis showed no significant association between gender and histological tumor type ($P=0.294$). Similarly, age group (≤ 7 years vs. >7 years) was not significantly associated with tumor type ($P=0.455$). Regarding anatomical distribution, 8 masses (47.1%) were located in the posterior mediastinum, 6 masses (35.3%) in the middle mediastinum, and 3 masses (17.6%) in the anterior mediastinum. In addition, 12 children (70.6%) were ≤ 7 years old, whereas 5 (29.4%) were older than 7 years. The frequency distribution of mass type according to anatomical location is presented in Table 1. Regarding histological classification, nine tumors (53%) were benign, eight (47%) were malignant, and one (6%) showed inflammatory features suggestive of infection (Caseating granulomatous inflammation). Chi-square analysis demonstrated a statistically significant difference in the frequency distribution of mass type according to anatomical location among the children studied, as neurogenic tumors were observed only in the posterior mediastinum.

The results showed no statistically significant difference in the frequency distribution of mass type according to gender, age, or initial symptoms in the children studied ($p=0.294$ and $P=0.455$, $P=0.251$ Chi-square test). Using the Log-rank test, mean survival time did not differ significantly according to surgery ($P=0.222$), type of malignancy ($P=0.158$), age (0.877), gender (0.670), or radiotherapy treatment (0.752). No difference was found in mean survival time according to surgery or type of malignancy in children ($P\text{-value}>0.05$). Similarly, no significant association was observed between mean survival time and the neurological origin of the tumor or chemotherapy treatment in the studied samples (7.15 ± 0.69) (Tables 2 and Figure 1).

Table 1. Frequency of mass type according to anatomical location

Mass type	Mass location			Total
	Posterior mediastinum (%)	Middle mediastinum (%)	Anterior mediastinum (%)	
Ganglioneuroma	5 (100)	0 (0)	0 (0)	5 (100)
Ganglioneuroblastoma	3 (100)	0 (0)	0 (0)	3 (100)
Hemangioma	0 (0)	0 (0)	2 (100)	2 (100)
Lymphoblastic lymphoma	0 (0)	1 (100)	0 (0)	1 (100)
Pleuropulmonary blastoma	0 (0)	1 (100)	0 (0)	1 (100)
Lipoblastoma	0 (0)	0 (0)	1 (100)	1 (100)
Caseating granulomatous inflammation	0 (0)	1 (100)	0 (0)	1 (100)
Rhabdomyosarcoma	0 (0)	1 (100)	0 (0)	1 (100)
Lymphoepithelial like carcinoma	0 (0)	1 (100)	0 (0)	1 (100)
Lymphoblastic lymphoma	0 (0)	1 (100)	0 (0)	1 (100)
Total	8 (47.1)	6 (35.3)	3 (17.6)	17 (100)
P-value	0.013			

Table 2. Survival time based on tumor origin (Neurogenic, Non-Neurogenic) in children*

Origin of tumor	Number of cases	Number of deaths	Mean survival time $\pm$ SD	P-value
Neurogenic	8	3	6.30 $\pm$ 0.80 years	0.666
Non-Neurogenic	9	2	7.46 $\pm$ 0.95 years	
Total	17	5	7.15 $\pm$ 0.69 years	

The P-value of 0.666 indicates no statistically significant difference between the groups.

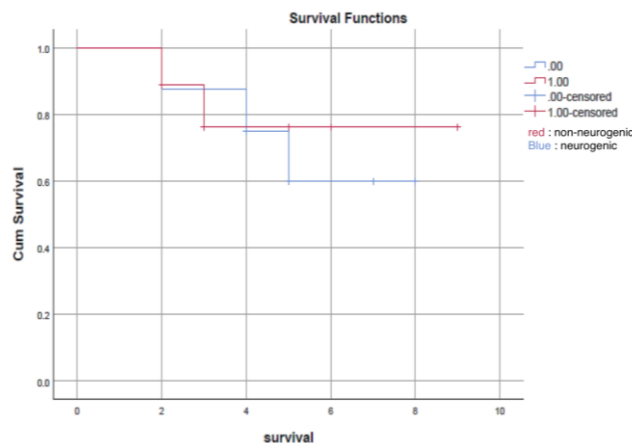


Figure 1. Kaplan-Meier survival analysis according to tumor origin (Neurogenic and Non-Neurogenic)

Discussion

Previous studies have indicated that mediastinal tumors in adults are predominantly asymptomatic (8). For example, Biko et al., in a study of 29 mediastinal tumors, reported that most patients were either asymptomatic or presented with nonspecific symptoms during diagnostic evaluation (3). In the present study, the most frequently reported presenting symptom was cough (23.5%). Another study reported that 41.6% of patients with mediastinal tumors were asymptomatic. However, cough, fever, and dyspnea are more commonly observed in pediatric cases than in adults, whereas symptoms more frequently reported in adults include chest pain or heaviness (4). A pediatric-focused study by Seth et al. (2017) identified nonspecific symptoms, including fever, night sweats, and weight loss, as well as secondary manifestations caused by local invasion or compression of mediastinal structures, such as respiratory distress and cough, as the most common clinical presentations (9). Similarly, Ahmadi et al. reported cough as the most prevalent clinical symptom (44.4%) and fever as the most common clinical sign (52.9%) (10). These findings are consistent with those of the present study and collectively suggest that mediastinal tumors are more often symptomatic in children than in adults. Regarding gender distribution, 70.6% of the children in the current study were female and 29.4% were male. Previous studies evaluating gender distribution among patients with mediastinal masses have yielded inconsistent findings. A 2020 study reported a predominance of women among patients with mediastinal masses (2). Similarly, Verma et al. reported a higher frequency of mediastinal tumors in women (11), which is consistent with the higher female predominance observed in the present study. In contrast, Ahmadi et al. reported an equal incidence in both genders among children (10), whereas Seth's study of 58 children with mediastinal tumors found that 77.5% of affected children were male (9). Taken together, these divergent findings suggest that no consistent gender predilection can be assumed for mediastinal masses, whether in pediatric or adult populations. With respect to age at onset, 70.6% of children in the present study were under 7 years of age. Liu et al. reported that the predominant age group at onset was children younger than 10 years (4). In Seth's study of 58 children, the mean age for mediastinal malignancies was 6.63 years (9). A separate 2007 study conducted in Iran reported that mediastinal tumors occurred across an age range of 17 days to 13 years, with the highest incidence observed in infants under 1 year of age (8). Furthermore, Ahmadi et al. documented that the highest prevalence of mediastinal tumors occurred between the ages of 5 and 10 years (38%) (10). The findings of the present study are therefore consistent with previous research, suggesting that the highest incidence of mediastinal tumors in pediatric populations occurs in children younger than 10 years.

In the present study, 8 masses (47.1%) were located in the posterior mediastinum, 6 masses (35.3%) in the middle mediastinum, and 3 masses (17.6%) in the anterior mediastinum. In another study of 105 patients, 63.8% of masses were located in the anterior mediastinum, 22.9% in the posterior mediastinum, and 13.3% in the middle mediastinum. Consistent with our findings, Verma et al. (2020) reported that the posterior mediastinum was the most common anatomical site of mediastinal tumors in children. In contrast, Ahmadi et al. (2004) reported anterior mediastinal masses as the most frequent in children (10,11). Overall, these findings suggest that the anatomical distribution of mediastinal masses may be influenced by the study population and tumor composition; adult series more frequently report anterior mediastinal involvement, whereas pediatric series may show a greater proportion of posterior or middle mediastinal tumors. In the present study, 53% of tumors were benign and 47% were malignant. The most common tumors were ganglioneuroma, ganglioneuroblastoma, and hemangioma, with frequencies of 29.4%, 17.6%, and 11.8%, respectively. Liu et al. (2017), in comparing lesion types between children and adults, concluded that neurogenic tumors, germ cell tumors, mesenchymal tumors, and lymphatic lesions were more common in children than in adults, whereas thymic lesions and metastatic carcinomas occurred more frequently in adults (8). In the study by Ahmadi et al. (10), lymphoma was the most common mediastinal mass (35.2%), followed by tumors of neural origin. Regarding survival and its associated factors in the present study, the average survival duration was 7.15 years, and none of the evaluated

variables, including age, sex, treatment type, and mass location, affected the average survival of children with mediastinal masses. Choe et al. (2022) reported that 76% of children with mediastinal tumors had favorable outcomes after an average of 6.2 months (12). Hodgkin's lymphoma and B-cell leukemia showed promising response rates of 87% and 66%, respectively, indicating a better prognosis than T-cell leukemia and metastatic neuroblastoma, each with a 50% favorable response. Children with superior mediastinal syndrome (SMS) had a relatively poorer prognosis, with a survival rate of 67%, compared with 83% among patients without SMS. In the study by Ahmadi et al. (10), the survival rate was 54% over an average follow-up period of 3.2 years.

Conclusion

The findings of this study suggest that the frequency distribution of histological types of primary mediastinal masses in children is mainly influenced by anatomical location. Statistical analysis showed that age, sex, treatment type, and tumor location were not significantly associated with survival among children with primary mediastinal tumors.

Strengths and limitations

Strengths: This study provides a comprehensive clinicopathological overview of primary mediastinal masses in a pediatric cohort from a single tertiary center, with long-term survival tracking using robust statistical methods, including Kaplan-Meier and Log-rank tests. Census sampling also ensured that all eligible cases over a 10-year period were included.

Limitations: The retrospective design and small sample size ($n=17$) limit the generalizability of the findings. Because this was a single-center study conducted in a specific region (Yazd, Iran), the results may not fully reflect broader populations. In addition, detailed molecular data were not available for all cases.

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Ethical Statement

This study was approved by the Ethics Committee of the School of Medicine at Shahid Sadoughi University of Medical Sciences, Yazd, Iran, under ethical code IR.SSU.MEDICINE.REC.1399.273.

Conflicts of Interest

All authors have no conflicts of interest to disclose.

Author Contributions

Mahlagha Zahedi, as the first and corresponding author, designed the study, supervised data collection, performed the statistical analysis, and drafted the manuscript. Sahar Abbasinia, as the second author, contributed to data collection, the literature review, and manuscript preparation. All other authors participated in data interpretation and critical revision of the manuscript for intellectual content. All authors approved the final version of the manuscript.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Use of Artificial Intelligence

The authors confirm that no artificial intelligence tools were used in the writing, analysis, or preparation of this manuscript.

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